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ACUTE INTERMITTENT PORPHYRIA – A CASE REPORT

AKUTNA INTERMITENTNA PORFIRIJA – PRIKAZ SLUČAJA

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Abstract

**Introduction.** Acute intermittent porphyria is rare inherited metabolic disorder caused by decreased level of porphobilinogen deaminase. Subsequently accumulation of byproducts in neural elements causes classic triad of abdominal pain, neurological dysfunction and psychiatric disturbances. **Case report.** We admitted in our intensive care unit a 22 year old female patient with convulsions, episode of blindness and progressive development of quadriparesis, bulbar paralysis and respiratory failure twelve days after colon resection in local hospital. Diagnosis was confirmed by high level of porphobilinogen in urine. Previous use of oral contraceptives, antidepressants and thiopenthal as induction agent for general anesthesia might be a precipitating factors. She was managed conservatively with high carbohydrate intake and human hemin and six months after admission transferred to department of rehabilitation. **Conclusion.** Early recognized acute intermittent porphyria is cornerstone of positive outcome. Second step is adequate therapy followed by prevention of attacks.

**Key words:** porphyrias, porphobilinogen, quadriplegics.

Apstrakt

**Uvod.** Akutna intermitentna porfirija je redak nasledni metabolicki poremećaj uzrokovani nedostatkom porfobilinogen deaminaze. Posledično nakupljanje međuproizvoda u nervnim strukturama dovodi do trijasa kliničkih simptoma bola u trbuhu, neuroloških ispada i psihijatrijskih poremećaja. **Prikaz bolesnika.** Primili smo u našu jedinicu intenzivnog lečenja 22-godišnju pacijentkinju sa konvulzijama, epizodom slepila i progresivnim razvojem kvadripareze, bulbarne paralize i respiratorne insuficijencije, dvanaest dana nakon resekcije delobog creva u lokalnoj bolnici. Dijagnoza je postavljena visokim nivoom porfobilinogena u mokraći. Prethodna upotreba oralnih kontraceptiva, antidepresiva i tiopentala kao indukcionog agensa u opštoj anesteziji mogli bi biti precipitirajući faktori. Lećena je konzervativno visokim unosom ugljenih hidrata i humanim heminom i šest meseci nakon prijema biva prebačena na odeljenje fizičke medicine i rehabilitacije. **Zaključak.** Postavljanje rane dijagnoze je osnovni korak uspešnog lečenja napada akutne...
intermitentne porfirije. Sledeći korak podrazumeva adekvatnu terapiju, praćenje i prevencijom nastanka ponovnih napada.

**Ključne reči:**
porfirija, porfobilinogen, kvadriplegija.

**Introduction**

Porphyrias are rare inherited or acquired disorders caused by partial deficiency of enzymes in the biosynthesis of heme. There are cutaneous and neurological forms of disease. However if we look generally, the disease is a result of enzyme dysfunction of same biosynthetic pathway, but differences in organ affection are from mistakes in different isoenzymes of one enzyme, different processing of mRNA and different microenvironment in cell matrix. Acute intermittent porphyria (AIP) is rare autosomal dominant disorder. Prevalence in Europe is 1-2 per 100 000 (highest is in Scandinavia with 1 per 1500).

**Case Report**

From local hospital we admitted 22 year female patient under suspicion for developing sepsis. The patient underwent trasversal colon resection twelve days earlier. On admission she was awake, had brief periods of confusion, dyspneic with SpO₂ 85% on room air, TA 160/100 mmHg, HR 140/min, BT 37,7⁰C, CVP 6 cmH₂O, abdominal pain, active peristalsis, intestinal contents visible on stoma, in urine bag light yellow urine. Laboratory values: SE 47, CRP 119, Leukocytes 17,4, arterial gas analysis pH=7,38, PaCO₂=52 mmHg, PaO₂=119 mmHg, HCO₃=30,8 mmoll/L.

After admission, patient had episodes of epileptiform seizures that lasts for few minutes and they were accompanied with apnea and complete loss of responsiveness. Computerized tomography (CT) of thorax, abdomen and pelvis revealed bilateral pleural effusions and pneumothorax on the right side which is drained with chest tube. After consultation with neurologist we did CT scan of head and EEG and EMNG. On the next day further deterioration with more episodes of convulsions, quadriplegia, bulbar paralysis, respiratory failure and eventually intubation and mechanical ventilation. We took blood cultures, smears and 24h collection of urine for porphobilinogen.
Brain CT scan revealed there were signs of suprasellar subarachnoid recession in to sella turcica and parenchymal cortical reduction frontally bilaterally. There were no areas of demyelization.

Electroencephalography (EEG) well expressed with minor diffuse dysfunction and elevated irritability of frontal regions bilaterally. Electromyoneurography (EMNG) findings - loss of conduction in proximal group of muscles with existing of spontaneous muscle activity and preserved sensory fibres. Finally, when results of porphobilinogen in urine arrived (904 µg/24h and normal values are less than 150 µg/24h) diagnosis of acute porphyria was made.

Hyponatremia, present from the beginning, was treated with 3% saline infusions and specific therapy with 10% and 50% dextrose IV along with enteral feeding and administration of Human hemin (Normosang® 25mg/ml, Orphan Europe SARL, Puteaux, France) in dose of 4mg/kg/day for four days in a row. Therapy with Normosang® was given on two occasions, after 30 days, and after three months. The first dose led to a minimal improvement in clinical symptoms, while the second dose had a better effect.

She was tracheotomised and percutaneous endoscopic gastrostomy has been done. After 160 days of intensive care she was transferred to the department of physical medicine and rehabilitation. The patient was discharge from intensive care with spontaneous breathing, with an act of swallowing and movements in all extremities (Figure 1, Figure 2).

Interviewing her parents we found out that at the beginning of the year she had laparoscopic surgery of ovarian cysts and subsequently received advice to take oral contraceptives (one of the main provoking factor). After just a few weeks she leaves stopped the suggested therapy because of nausea and vomiting, apathy and sleepiness. Three months later, she was hospitalized in a local hospital with significant epigastric pain and vomiting, back pain and constipation that lasts for four days. During hospital stay she has had also suffered from insomnia and hallucinations. Ward doctor consulted a psychiatrist who established diagnosis of somatoform disorder and prescribed her sulpiride (Eglonyl®, Alkaloid AD, N.Macedonia), one of porphyrinogenic drugs. After series of medical tests and examinations she has been discharged with the diagnosis of biliary gastritis. Next day, at the request of her parents she was admitted to a higher-level hospital in the nearby town due to further worsening of the abdominal pain and the appearance of
new symptom- inability to climb the stairs (due to proximal neuropathy). CT scan of abdomen revealed widening of transverse colon which is interpreted as toxic megacolon and she underwent surgery. After twelve days later she was transferred to our hospital.

Discussion

Acute Intermittent Porphyria (AIP) symptomatic is mainly heterozygotes and rarely homozygotes. It is characterized by long latent period and symptoms become manifested after puberty in third and fourth decade of life after exposure to some provoking factor. There are no cutaneous manifestations. AIP is metabolic disorder caused by deficiency of porphobilinogen deaminase (PBGD). Patients with AIP have acute attacks of neurovisceral symptoms (affection of autonomic nervous system) followed with high level of porphyrin precursors in urine. First presentation of disorder is in 85-95% abdominal pain and in 45% peripheral neuropathy with motor weakness. Exact mechanism of neuronal damage is unknown, one of proposed theory is crystallization of byproducts in neural structures.

Variety of clinical presentation is considerable: abdominal pain, nausea, vomiting, paralytic ileus, urinary retention or incontinence, tachycardia, arterial hypertension, sweating, tremor, postural hypotension, peripheral neuropathy (proximal because of axonal degeneration and demyelination), sensory neuropathy (paresthesias and dysesthesias), cranial neuropathy (VII and X), periodical cortical blindness (caused by vasospasm), epileptiform seizures and rarely bulbar paralysis and death.

Deficiency of PBGD is not enough for clinical manifestation there must be a presence of provoking factors: medications (inductors of P450 cytochrome oxidase), fasting, hormones (progesterone), smoking, alcohol, metabolic stress (infection, surgery, psychological stress)

Diagnosis is based on clinical presentation and high level of urine porphobilinogen. The most relevant thing is high level of clinical suspicion.

Treatment consists of following steps: review all medications and discontinue any that can exacerbate acute porphyria, restore energy balance using an enteral route if possible if not IV dextrose in dose of 300-400 g/day, hemin 3-4 mg/kg IV, given once daily for four days
and prevention of future attacks (treat intercurrent infections and other diseases promptly)\textsuperscript{11, 12}.

Chronic complications are hepatocellular carcinoma and renal failure\textsuperscript{13, 14}.

**Conclusion**

AIP has capability for mimicking wide variety of medical conditions. It is important to have high index of clinical suspicion and then with relatively simple biochemical test to confirm diagnosis of AIP. Specialized care and prevention of future attacks are cornerstones of favorable outcome. Nevertheless, we need more research in the future in order to obtain new therapeutic opportunities as well as detection of parameters for monitoring the effects of therapy and prediction of outcome.

**Literature:**


Prilog:
Figure 1. Patient on discharge from intensive care

Figure 2. Patient with renewed movements in the extremities